Allergy Abstracts

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Asthma and Hay Fever

Effects of Acute Anoxia on the Circulation and Respiration in Patients With Chronic Pulmonary Disease Studied During the "Steady State." Fishman, A. P., McClement, J., Himmelstein, A., and Cournand, J.: J. Clin. Investigation **31**: 770, 1952.

The effects of acute anoxia on the circulation and respiration were carefully studied in 35 patients with such pulmonary diseases as bronchiectasis, diffuse infiltrations of unknown cause, scleroderma, silicosis, miliary or chronic pulmonary tuberculosis, Boeck's sarcoidosis, beryllium fibrosis, bronchial carcinoma with emphysema, and bronchial asthma with chronic emphysema. All except 3 subjects had higher than normal respiratory minute volumes.

When oxygen concentration of the respired air was increased, ventilation showed little change, carbon dioxide levels in plasma showed "no consistent direction of change," heart rate usually slowed or remained unchanged, cardiac output either did not change or decreased, and the mean pulmonary artery pressure was unaffected, except in 2 instances where an increase of 8 mm. Hg was noted. Brachial artery pressure remained stable.

When mixtures of less than 21 per cent oxygen were administered, the volume of ventilation increased and arterial plasma carbon dioxide decreased. During exposure to low oxygen, 7 of 28 patients exhibited persistent tachycardia. At low levels of oxygenation, cardiac output either showed little change or increased (in relation to decreased arterial plasma oxygen tension), mean pulmonary artery pressure increased, particularly in those patients with simultaneous increases in cardiac output, and brachial artery pressure showed no consistent trend.

Particular emphasis is placed on the necessity for basal conditions and the achievement of a "steady state" prior to gathering experimental data. Detailed protocols are presented. K.

Relief of Status Asthmaticus by Continuous Intravenous ACTH Therapy. Lockey, S. D., Paul, J. D., Grosh, J. L., Griswald, A. S., and Stubbs, D. S.: Ann. Allergy **10**: 592, 1952.

ACTH was administered intravenously to 19 patients in status asthmaticus after the usual therapeutic procedures had failed to afford relief. The hormone was given in a solution of 5 per cent glucose in distilled water to which potassium chloride had been added. The rate of flow of the solutions was adjusted to 28 drops per minute, approximately one liter in twelve hours. Eighty milligrams of ACTH per day was the dosage used in the early part of the series, but it was soon observed that 40, 20, or even 10 mg., when given by the slow drip method, produced good results. Lengthening the period of administration, i.e., slowing the rate of the infusion, gave proportionately longer periods of relief. The adrenal cortical activity seemed to persist for approximately twice the time that it took to administer the solution. F.

Probable Role of Airborne Soil Bacteria in Perennial Hay Fever and Asthma. Dutton, L. O.: Ann. Allergy **10**: 615, 1952.

Dust storms in the El Paso, Texas, area appeared to produce severe symptoms in certain hay fever and asthma patients while other patients were apparently unaffected. From this observation, it became apparent to the author that air-borne soil bacteria might be an important etiologic factor. Vaccines were prepared from bacterial cultures grown on plates exposed during sand storms. A series of approximately 400 patients were skin tested with various dilutions of these vaccines. About 5 per cent of those patients who were unaffected by the sand storms gave positive immediate skin reactions, whereas 80 per cent of the patients whose symptoms were increased during the sand storms gave positive reactions. No true tuberculin-type reactions were observed in the series. Among a group of 75 patients treated with the bacterial suspensions, about 50 per cent experienced apparent clinical improvement. F.

Psychology of Asthma. Edgell, P. G.: Canad. M. A. J. **67**: 121, 1952.

The author discussed the frequency with which emotional episodes appeared to precipitate asthmatic attacks in patients under his care. The inability of most allergists to diagnose the etiologic factors producing asthma in about 20 per cent of their cases suggested the possible influence of psychogenic factors in these cases. Most asthmatics were found to have deep-seated emotional insecurity and a strong need for parental love and protection. Asthmatic attacks in some patients were found to be associated either with psychic disturbances or with psychoneurotic manifestations. Asthma as a result of suppressed emotion, especially rage or anger, was commonly observed. The author stressed the importance of psychiatric therapy in certain asthmatic patients and the significant improvement which often occurs from such therapy. R. W.

Dermatology

Wool as a Cause of Eczema in Children. Hill, L. W.: New England J. Med. **245**: 407, 1951.

Observations were made on 40 children between the ages of 2 and 12 years with "winter eczema." Most of the patients were atopic. Intracutaneous tests were made with a wool extract containing 0.01 mg. of nitrogen. For patch tests, a wet piece of white "all-wool" blanket was applied, after scraping the skin with a tongue depressor to remove part of the protective

keratin layer. Patch tests were read at the end of one week. Five patients showed positive reactions to both intracutaneous and patch tests, 5 showed positive reactions to the intracutaneous test but negative to the patch test, and 9 showed a positive patch but a negative intracutaneous reaction. All positive patch reactions were of clinical significance; the importance of the positive intracutaneous reactions was questionable. The author states that sensitivity to wool is common, is easily demonstrable, and is frequently the only cause for "winter eczema." House dust was reported as another cause of this type of eczema. Avoidance of wool, application of salves and pastes, and protection of the involved parts from external irritation by means of cotton cloth and an elastic bandage are considered important measures. Although eczema is most often caused by contact, inhalation may also play a role.

Hyposensitization therapy was successful in 3 patients, ranging from 5 to 15 years, who had had severe incapacitating eczema for about five years. Their case histories and treatment are given in detail. The author states that hyposensitization therapy is worth a trial only in the most severe cases.

I. Glazer.

Thrombotic Thrombocytopenic Purpura. Gendel, B. R., Young, J. M., and Kraus, A. P.: Am. J. Med. **13**: 3, 1952.

Thrombotic thrombocytopenic purpura is characterized by the clinical triad of hemolytic anemia, thrombocytopenic purpura, and central nervous system involvement. The clinical course is usually acute with sudden onset of fever, weakness, pallor, jaundice, and hemorrhagic manifestations. The disease usually runs a rapid, fatal course. Although the etiology of the disease is unknown, hypersensitivity has been suspected as a cause and, in certain reported cases, suspicion has been centered on penicillin sensitivity. Two cases of the disease are presented. **F.**

Papular Urticaria. Its Relationship to Insect Allergy. Shaffer, B., Jacobson, C., and Pari, P. P.: Ann. Allergy **10**: 411, 1952.

Previous studies by various investigators have suggested that the bites of many insects, including bedbugs, fleas, and mosquitos, are important etiologic agents in papular urticaria. This skin condition is usually observed in children between the ages of 2 and 7 years and occurs principally during the warm months of the year. Histologically there is a marked similarity between the various types of lesions found in papular urticaria and the corresponding lesions of insect bites. Skin testing with various insect allergens elicits a high percentage of reactions of both the immediate and delayed types in patients with papular urticaria, whereas normal individuals only occasionally show positive immediate reactions and almost never show positive delayed reactions. A high percentage of patients treated by the local application of 5 per cent D.D.T. in talc were "cured" of papular urticaria within a period of two weeks. **F.**

Fixed Drug Eruption Due Both to Aureomycin and to Terramycin. Report of a Case. Dougherty, J. W.: Arch. Dermat. & Syph. **65**: 485, 1952.

Urticarial violaceous pruritic plaques appeared on the dorsal surfaces of the hands, feet, and penis of a 29-year-old male, following the ingestion

of 0.5 Gm. of Aureomycin. The eruption disappeared forty-eight hours after the medication was discontinued leaving hyperpigmented macules. He had received a course of Aureomycin two and four months previously without any ill effects. Two months later the ingestion of Aureomycin was followed by the appearance of urticarial lesions at the sites of the residual hyperpigmented macules. The drug was discontinued and the urticarial component disappeared leaving again the excess pigment deposition. Ten days later, terramycin therapy in the same dosage resulted in a recurrence of the urticarial element in exactly the same sites. C.

Failure of Pyromen to Affect the Development of an Eczematous Sensitization in the Guinea Pig. Rostenberg, A., Jr.: J. Invest. Dermat. **18**: 311, 1952.

Six guinea pigs were given intraperitoneal injections of 0.1 gamma of Pyromen in 0.5 c.c. of fluid, 3 times weekly for two weeks. In order to give this dose, commercial Pyromen was diluted 1:50 with saline. A similar group of animals was treated in the same manner with the commercial solvent used to dissolve Pyromen. Both groups of guinea pigs were then exposed repeatedly to sensitizing doses of 2:4 dinitrochlorobenzene and tested for possible sensitivity two weeks later. There was no difference in the incidence of eczematous contact sensitivity in the treated group and in the control group. The author concludes that Pyromen is ineffective in preventing eczematous sensitization to 2:4 dinitrochlorobenzene in the guinea pig. R. W.

Eczematous Sensitization Via the Lymphatic Glands Compared With Other Routes. A Study of 2-4 Dinitrochlorbenzene. Seeberg, G.: Acta dermat.-venereol. **31**: 592, 1951.

Confirming the results reported by other workers, the writer found that eczematous sensitization is more readily achieved by the epicutaneous and intracutaneous sensitization routes than by subcutaneous injections.

Injection into a lymphatic gland was found to result in sensitization to a degree equal to that obtained by the epicutaneous and intracutaneous routes. H.

Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of the Skin. II. Allergic and Other Dermatoses; Report of 67 Cases. Hopkins, J. G., Kesten, B. M., Nelson, C. T., Hambrick, G. W., Jr., Jennings, R. G., Jr., and Machacek, G. F.: Arch. Dermat. & Syph. **65**: 401, 1952.

Sixty-seven patients with cutaneous eruptions were treated with corticotropin (ACTH) and cortisone. There were 42 cases of allergic dermatoses including 8 cases of allergic eczema, 3 cases of urticaria not produced by drugs, 21 cases of drug eruptions, and 10 cases of dermatitis venenata. Beneficial and dramatic results were obtained in patients with drug eruptions, urticaria, and dermatitis venenata. The drugs were of temporary benefit in the treatment of atopic eczema. No benefit was obtained in the treatment of solar urticaria, dermatomyositis, keratoconjunctivitis sicca, and *Psoriasis arthropathica.* The dosage of the drugs and the side effects observed are discussed. C.

Otorhinology and Ophthalmology

Biochemical Aspects of Nasal Polyps. Baldwin, J. L.: J. Lab. & Clin. Med. **39**: 737, 1952.

Nasal polyps removed from 31 patients were anlyzed chemically in an effort to learn more about their pathogenesis. Water, chloride, sodium, potassium, calcium, magnesium, and total nitrogen determinations were performed on the wet polyp tissue and on dry polyp solids. When the constituents of these polyps were compared with those of other soft tissues it was found that the nasal polyps contained high concentrations of chloride and sodium and a low concentration of potassium. Therefore, the salt concentrations in polyps were characteristic of body fluids and not of soft tissues. The sodium: chloride ratio in polyps closely approximated that in serum. In comparing the protein, potassium, and magnesium content of polyps with other soft tissues, the polyp concentrations of these substances were low, indicating a small cellular phase or low cell mass. The cellular constituents, nitrogen, potassium, and magnesium, when expressed in 100 Gm. of dry solids for each polyp specimen, were very constant and indicated that the cells were of the same composition in each tissue. Total nitrogen determinations of nasal polyp fluid approximated those of antrum cyst fluid. From the biochemical point of view, the fluids of nasal polyp masses were similar to those of antrum cyst fluids in electrolyte and nitrogen content. The sodium:chloride ratio in both fluids was the same as that in blood, indicating the presence of a phase in both fluids similar in composition to blood. This suggested the possibility that the same pathologic conditions foster the formation of both phenomena. E. W.

The Nasal Mucosa of Allergic Patients Before and After Treatment With Corticotropin. Rappaport, B. Z., Samter, M., Catchpole, H. R., and Schiller, S.: Ann. Otol. Rhin. & Laryng. **61**: 909, 1952.

Nasal mucosa was obtained by biopsy during the hay fever season in 32 ragweed-sensitive patients before and four days after treatment with ACTH. When compared with the nasal mucosa removed before treatment, the following changes were noted. There was a general increase in stainability of the glycoprotein ground substance and in the staining density and width of the basement membrane. The cement substance between the epithelial cells of the mucosa increased in size. There was an increase in the number and size of red-staining granules in the cytoplasm of stellate, oval, and round cells present in the submucosa. It is assumed that during the allergic reaction the glycoproteins of the ground substance and the basement membranes are broken down (depolymerized) to smaller units with a proportionate loss in stainability. The effect of corticotropin is to arrest the process of depolymerization. The glycoproteins are restored to the normal state with a resultant increase in stainability. C.

Miscellaneous Allergies

The Insect Bite Reaction. II. Evaluation of the Allergic Reaction. Rockwell, E. M., and Johnson, P.: J. Invest. Dermat. **19**: 137, 1952.

Mosquito bite reactions were studied in the following groups of patients: newborn babies; employees of the United States Department of Agriculture, Bureau of Entomology and Plant Quarantine, Orlando, Fla.; subjects with no history of severe reactions to mosquito bites; and patients with severe mosquito bite reactions. The entomologists were known to have been previously exposed to specific species of insects. Extracts were prepared from

Culex pipiens, Aedes aegypti, and *Anopheles kuadrimaculatus* by techniques similar to those employed in the preparation of allergenic extracts. By animal experiments the extracts were found to be toxic in high concentrations. In the experience of the writers, however, an immediate and/or delayed reaction to an intracutaneous test with a 1:100,000 or a 1:1,000,000 dilution of the extract or a positive patch test to 1:10 or 1:100 dilution of the extract was regarded as evidence of hypersensitivity to mosquitoes. Immediately following a bite from *A. aegypti,* newborn babies developed small petechial reactions followed by small papules. The entomologists and technicians showed very mixed responses. Some reacted only to the species to which they had been exposed, while others who had been exposed to many species reacted only to a few of them. As a rule, the degree of response following a bite paralleled the degree of skin test reaction. Many patients with severe mosquito reactions gave positive personal and/or family histories of allergy. Three types of allergic reactions to mosquito bites were observed, namely, urticarial, tuberculin-like, and eczematoid. These reactions could be duplicated experimentally by intracutaneous or patch tests with crude mosquito extracts. The urticarial type of sensitivity can occasionally be transferred passively. The authors found it difficult to find suitable receptors for passive transfer studies and state that this difficulty is due to the fact that many individuals do not react. It was concluded that small mosquito bite reactions can result from irritation alone, but that some reactions are allergic in nature. There is also evidence that multiple antigens are involved in the mosquito bite reaction. R. W.

ACTH in the Treatment of Multiple Wasp Stings. James, E. S., and Walker, W. G.: Canad. M. A. J. **67**: 50, 1952.

The authors observed a child, 18 months old, who had received at least 477 separate wasp stings. The youngster was in partial shock, severely edematous, and practically anuric during the first twenty-four hours of hospitalization. He was given sedation, analgesics, and adrenalin on admission. Eight hours later, intramuscular ACTH therapy was started, 10 mg. for the first dose and 5 mg. every six hours thereafter. The youngster started to improve during the next twenty-four hours and within forty-eight hours had a normal blood pressure, was voiding freely, and was apparently out of danger. In view of the number of drugs which he had received, no definite conclusions were drawn concerning the value of ACTH in the over-all therapeutic program. It is suggested, however, that ACTH therapy should be started as soon as possible following multiple insect bites. R. W.

Induced Sensitivity From the Vaginal Use of a Sulfonamide Jelly. Incidence as Determined by Patch and Oral Tests. Branscomb, L.: Am. J. Obst. & Gynec. **63**: 175, 1952.

The incidence of sensitivity to sulfonamide preparations used locally in the vagina was investigated. Previous reports have indicated that sensitivity to the drug may develop when it is administered by this route.

In the present study, 250 women were given preliminary patch tests with sulfathiazole. Two women with positive patch reactions gave a history of previous sulfonamide reactions, and were eliminated from the study. The remainder of the patients were then given 0.5 Gm. of sulfathiazole orally. A lighting up of the site of the patch test within eight hours would have been regarded as evidence of sensitivity; however, this did not occur in any of the patients.

Two hundred women with negative patch and ingestion reactions were treated with 0.25 ounce of 10 per cent sulfathiazole ointment which the patient inserted into the vagina nightly for from twenty-four to thirty-six days. The sensitivity tests were repeated on each patient at the end of the treatment period. None showed positive patch reactions. One patient showed clinical evidence of having been sensitized. After the sixth treatment, she developed joint pains, swelling of the hands and feet, and erythema nodosum-like nodes.

The incidence of induced sensitivity (0.5 per cent) in this study was so low that there seems to be no contraindication to the use of this form of therapy where indicated. J. S.

Anaphylaxis

Anaphylactic Shock in the Pertussis Vaccinated Mouse. Malkiel, S., and Hargis, B. J.: Proc. Soc. Exper. Biol. & Med. **80**: 122, 1952.

White mice were sensitized by the intraperitoneal injection of *H. pertussis* vaccine and horse serum. On the fourth day after sensitization, a series of sensitized and control animals were injected with histamine intraperitoneally. The LD_{50} of histamine diphosphate for the control group of mice was fifty times greater than that for the vaccinated mice. Fifteen days after sensitization, 102 vaccinated mice were injected intravenously with horse serum and 95 died in anaphylactic shock. When 66 mice, sensitized to horse serum without *H. pertusis* vaccine were challenged with horse serum, 3 died in shock. These experiments were repeated with several other vaccines. Only *Brucella abortus* vaccine demonstrated the enhancement of anaphylactic sensitivity similar to that shown by *H. pertussis* vaccine. B.S.

The Effect of Cortisone on the Shwartzman Reaction. The Production of Lesions Resembling the Dermal and Generalized Shwartzman Reactions by a Single Injection of Bacterial Toxin in Cortisone-Treated Rabbits. Thomas, L., and Good, R. A.: J. Exper. Med. **95**: 409, 1952.

The administration of large doses of cortisone from two to four hours prior to the intravenous injection of toxin has been found to inhibit the development of the Shwartzman reaction. Further studies were made on rabbits which were injected with 25 mg. of cortisone daily for four days. On the third day, *S. marcescens* toxin was injected intracutaneously and on the following day, four hours after cortisone injection, each animal received the toxin intravenously. Shwartzman reactions developed in all animals. During the first twelve hours after the intracutaneous injection of toxin, local skin reaction was absent in treated animals, whereas the controls exhibited local erythema and edema in this period. From the eighteenth to twenty-sixth hours, if intravenous toxin was withheld, the cortisone-treated animals developed small petechiae in the injected skin. This did not occur in any of 40 controls. When 60 mg. of cortisone was administered intramuscularly two hours before the intravenous toxin challenge, Shwartzman reactions still occurred. Histologic studies of skin prepared for Shwartzman reaction by the initial injection revealed less inflammatory cell infiltration in the cortisone-treated animals, but many thrombi composed of leukocytes and platelets were present in the blood vessels of the area in marked contrast to the unaffected blood vessels of the controls. The possibility that these effects might have been caused by a cortisone-induced blood stream infection was investigated by means of blood culture studies. These were negative. The initial intracutaneous injection of toxin normally decreases skin permeability to trypan blue dye. Cortisone administration failed to alter this

finding despite the absence of local erythema or edema in the injected area of animals so treated. Cortisone likewise did not affect the usual local increase in lactic acid or the degree of aerobic production of lactic acid when prepared skin samples were compared with normal skin tissues from the same animals. The administration of nitrogen mustard in a manner which inhibited the Shwartzman reaction also inhibited the primary hemorrhagic reaction to toxin in cortisone-treated animals. This effect could be correlated with the production of leukopenia in the same manner as has been previously observed in the Shwartzman phenomenon, namely, the fewer circulating polymorphonuclear cells the less the vascular damage.

The generalized Shwartzman reaction, characterized by bilateral cortical necrosis of the kidneys, is usually produced by two intravenous injections of bacterial toxin spaced twenty-four hours apart. Rabbits injected with 25 mg. of cortisone daily for four days were subjected to a single intravenous injection of *S. marcescens* toxin on the third day. Within twenty-four hours, most of the animals exhibited weakness and respiratory distress. Half of the animals died and the remainder were sacrificed at the end of thirty hours. ". . . bilateral cortical necrosis of the kidneys was present in 70 per cent of the rabbits . . . , with accompanying hemorrhagic lesions of the lungs, spleen, liver, and gastrointestinal tract in most instances. Similar results were obtained in cortisone-treated rabbits with a single intravenous injection of meningococcal toxin, in a dose of 2 c.c. of a 1:10 dilution." Fifty controls given cortisone without toxin and 150 rabbits given toxin without cortisone were free of gross or microscopic renal lesions. Cultures of blood and kidney tissue in 12 rabbits with severe renal necrosis were negative. The renal lesions produced by toxin administered in the wake of cortisone were those of widespread parenchymal hemorrhage, and necrosis of glomeruli and tubules within the cortex. Rarely was there extension to the medulla. The glomerular capillaries were filled with homogeneous eosinophilic material which stained like a mucopolysaccharide. "Neither platelets, leucocytes nor erythrocytes could be demonstrated in the occluded glomerular capillaries." In comparing this with the conventionally produced generalized reaction, the lesions were indistinguishable, although intestinal hemorrhages tended to be more extensive than those of the cortisone-treated group. The degree of systemic leukopenia produced by intravenous toxin was virtually identical in the animals treated with cortisone and in the control animals not so treated. The administration of nitrogen mustard prior to the injection of toxin prevented the renal lesions from developing in the cortisone-toxin-treated animals as well as in those given the two intravenous doses of toxin. The protective effect of mustard was associated with polymorphonuclear leukopenia caused by this drug. Clamping off one kidney at the time nitrogen mustard was injected did not affect the results, indicating that the protective action of nitrogen mustard did not depend on exposure of the kidney to this poison. Clamping of the abdominal aorta to protect the femoral marrow at the time nitrogen mustard was administered inhibited the protective effect in both groups, the cortisone-treated animals, however, showing a less complete inhibition of protection than the group treated with two injections of toxin.

Unsuccessful attempts were made to elicit the generalized Shwartzman reaction in cortisone-treated rabbits and in animals pretreated with *S. marcescens* toxin by the subsequent injection of glycogen, kaolin, and, in sensitized animals, egg white.

It was next determined that intravenous doses of 0.4 mg. of *S. marcescens* toxin were the optimal amount required to induce renal necrosis in cortisone-treated rabbits, whereas doses of 0.2 mg. or less seldom produced the lesions. In untreated rabbits, 2 intravenous injections of 0.05 mg. consistently provoked

renal lesions. Eight cortisone-treated rabbits were then injected intracutaneously with 0.4 mg. of toxin. Seven developed renal lesions. Of 8 untreated rabbits injected intravenously with 0.4 mg. toxin, 4 were given 0.4 mg. intracutaneously twenty-four hours later and developed no lesions. The remaining 4 were injected with the same dose intravenously and all developed renal necrosis. None of 4 rabbits given 0.4 mg. of toxin intracutaneously followed by the same dose intracutaneously after twenty-four hours developed renal lesions. It was concluded that in cortisone-treated rabbits, intracutaneously injected toxin is absorbed so rapidly from the skin that the effect is renal damage comparable to that elicited by a similar amount of toxin administered by vein. There was no pathologic evidence of absorption of toxin from the intracutaneous site in animals not treated with cortisone, although the intracutaneous dose in these animals was 8 times greater than the intravenously effective dose.

It was concluded "that there is a close similarity, if not identity, between the skin and kidney lesions produced by a single injection of toxin in cortisone-treated rabbits and the lesions of the local and generalized Shwartzman phenomena." Several possible explanations for this effect of cortisone are discussed, including the possibility that cortisone treatment may reduce the capacity of lymphoid and other cells to remove or retain toxin from the circulating blood. K.

Pharmacology, Physiology, and Pathology

Immunochemical Studies of Antitoxin Produced in Normal and Allergic Individuals Hyperimmunized With Diphtheria Toxoid. I. Relationship of Skin Sensitivity to Purified Diphtheria Toxoid to the Presence of Circulating, Non-Precipitating Antitoxin. Kuhns, W. J., and Pappenheimer, A. M., Jr.: J. Exper. Med. **95**: 363, 1952.

A 6-year-old atopic boy developed a severe asthma attack within a few minutes after receiving a booster dose of diphtheria toxoid. Subsequent testing revealed immediate wheal reactions to minute intracutaneous doses of purified toxoid. The sensitivity was passively transferred. Serologic tests were unusual in that there was an antitoxic titre of 50 units per cubic centimeter, but no precipitating antitoxin.

Medical and dental students were divided into atopic and nonatopic groups and were Schick-tested with 0.1 ml. of diphtheria toxin in buffered heated human serum albumin and with both diphtheria toxoid and buffered human albumin as controls. The wheal and erythema reaction of the test site was compared with the control reactions after fifteen to thirty minutes. Serologic tests were also carried out for antitoxin titre and precipitin reactions. Forty of 131 students evidenced immediate reactions to toxoid; 35 of the 40 were classed as atopic individuals. Of 59 students who gave either a personal or familial history of atopy, "35 (60 per cent) showed wheal and erythema reactions to the toxoid used as Schick control and only slight or no immediate reaction to the tuberculin test . . . or to the diluent used on the Schick test." Only 5 (7 per cent) of 72 nonatopics showed slight or moderate skin sensitivity. There were twice as many such reactions among the Schick-negative subjects as among the Schick-positive subjects. All of the 11 students who showed 4-plus immediate reactions on initial testing were both atopic and Schick-negative. Following the booster dose immunization, 34 of 39 Schick-negative subjects developed some cutaneous reactivity to toxoid. After immunization the correlation between atopy and the cutaneous reaction to toxoid was much less striking and marked reactions were observed in nonatopic individuals. Both atopic and nonatopic individuals showed discrep-

ancies between the antitoxic reactivity of their sera on rabbit skin test and the specific precipitable antibody content, the latter antibody being "low" or absent in over one-third of the cases.

Apparently, reactions to peptones, which until recently have been used to stabilize Schick testing materials, have hitherto masked evidences of hypersensitivity to diphtherial proteins. Passive transfer test studies were not made with the sera of the experimental subjects. K.

Immunochemical Studies of Antitoxin Produced in Normal and Allergic Individuals Hyperimmunized With Diphtheria Toxoid. II. A Comparison Between Immunological Properties of Precipitating and Non-Precipitating (Skin-Sensitizing) Antitoxins. Kuhns, W. J., and Pappenheimer, A. M., Jr.: J. Exper. Med. **95**: 375, 1952.

Skin-sensitizing, precipitating, and nonprecipitating antibodies to diphtheria toxin were studied before and after the administration of a booster dose of diphtheria toxoid. Serial dilutions of serum were made and sites in Schick-positive (nonimmune) subjects were passively sensitized. Forty-eight hours later, the sites were tested with 0.1 Lf toxoid. Positive transfer reactions were obtained. With one serum, a thousandfold increase in serum reagin titre was noted, paralleling the antitoxin rise in the same serum from 0.06 to 60 units per cubic centimeter following booster immunization. Passive transfer experiments with sera from subjects who were not cutaneously sensitive to toxoid were negative. Only sera containing appreciable amounts of nonprecipitating antitoxin showed transferrable skin-sensitizing antibody. One serum containing 80 units of antitoxin per milliliter was obtained from an individual who exhibited a severe immediate wheal and erythema reaction to Schick control toxoid. Another serum containing 140 units per cubic centimeter of antitoxin was obtained from a person who showed only slight skin sensitivity to toxoid. In the former instance, no percipitating antibody was present and in the latter case 249 mg. per cubic centimeter of precipitating antibody was found. (Precipitating antibody in the amount of 2.5 mg. had been found to be equivalent to 1 unit of antitoxin in earlier studies.) Test tube mixtures of each of these sera with toxoid resulted in immediate cutaneous reactions on injection. Sites sensitized with the serum containing only nonprecipitating antibody remained reactive for over forty-five days. This serum failed to fix guinea pig complement in the presence of toxoid and neutralized the same amount of toxin whether the latter was added in portions or all at one time. Precipitating antitoxin fixes complement and even though serum containing precipitating antibody was heated so that precipitation no longer occurred, the Danysz phenomenon (maximal neutralization of toxin when added all at once) still occurred. Heating nonprecipitating antitoxin at 56° C. for four hours converts it to an antibody capable of blocking the wheal-erythema reaction of a passively sensitized site, when challenged by toxoid, and does not interfere with its ability to sensitize guinea pigs to anaphylactic shock nor with its antitoxic potency as determined by rabbit skin titrations. Precipitating antitoxin is also an anaphylactogen and inhibits the reaction of the passively sensitized site to certain mixtures of precipitating antitoxin and toxoid. Skin-sensitizing antitoxin was coprecipitated in the presence of toxin and precipitating antitoxin. No complement was present.

The resemblance of nonprecipitating human antitoxin to the atopic reagin is such that "it is suggested that the toxin-antitoxin reaction may provide a useful model for studying the type of immunological reactions encountered in allergic conditions of the hay fever type." K.

The Influence of Adrenal Cortical Extract on Immunological Phenomena in Vivo. I. Antigen-Antibody Reactions as Indicated by Hypocomplementemia, Granulocytopenia and Reduction of Circulating Antibody. Stavitsky, A. B.: J. Immunol. **69**: 63, 1952.

Rabbits were sensitized either to bovine gamma globulin (BCG) or to horse serum. Half of these animals were given injections of potent adrenal cortical extract (ACE) three hours prior to the injection of the specific antigen. Since it had been previously shown that both hypocomplementemia and granulopenia followed in vivo antigen-antibody reactions, the amount of complement and the number of granulocytes were employed as a measure of the amount of antigen-antibody union. It was found that ACE had no effect on the in vivo antigen-antibody reaction, as evidenced by the granulocytopenia and the fixation of complement. Rabbits were passively immunized with pneumococcus type III polysaccharide antiserum and then stimulated with antigen. Some of these animals received ACE before the sensitizing injection of antiserum. No difference in the granulocytopenia accompanying the passively induced antigen-antibody reaction was observed in the control and in the hormone-treated group.

High precipitin titres were produced in rabbits by the intravenous injections of alum-precipitated crystalline egg albumin. Using the method of Culbertson, quantitative antibody determinations were made and slightly less than the calculated amount of antigen required to fix the known amount of antibody was injected intravenously. Antibody determinations were made on the serums before and after the injection of the antigen. About one week later, the experiment was repeated at which time the rabbits were given ACE four hours before the antigen injection. It was found that "in every case the circulating antibody combined with close to the estimated amount of antigen." These experiments demonstrated more conclusively that ACE had no effect on antigen-antibody reactions. It is suggested that ACE exerts no direct action on the in vivo union of antigen and antibody, but probably affects the reactivity of mesenchymal tissues. R. W.

A Phagocytosis Inhibition Test in Infection Hypersensitivity. Merchant, D. J., and Chamberlain, R. E.: Proc. Soc. Exper. Biol. & Med. **80**: 69, 1952.

Polymorphonuclear leukocytes used in the test were obtained by stimulating the production of an exudate in the peritoneal cavity of normal guinea pigs. These cells were washed and diluted to a known concentration. The system used to test the phagocytic activity contained serum from animals sensitized to a Group B beta-hemolytic streptococcus or to a type I pneumococcus, and a filtrate of a twenty-four hour broth culture of the respective organism. A heat-killed suspension of *Bacillus anthracis* was the material to be phagocytized. In performing the test, 0.3 ml. of the sensitized serum was mixed with 0.1 ml. of the filtrate and 0.1 ml. of the leukocyte suspension and the tubes were incubated with continuous agitation for fifteen minutes at 37° C. Then 0.1 ml. of anthrax suspension was added and a drop of the mixture was placed on a glass slide. After another fifteen-minute period of incubation, the slide was examined with dark-field illumination or a phase contrast microscope. The percentage phagocytosis was calculated by dividing the number of cells containing bacteria by the total number of cells counted and multiplying by 100. The combination of streptococcal filtrate and sensitized serum caused a 10 per cent decrease in phagocytic action. This was considered statistically significant. A similar inhibition of phagocytosis was obtained with pneumococcal filtrate and sensitized serum. The specificity of the reaction was demonstrated by the failure of the mixture of sensitized serum

and heterologous filtrate to inhibit phagocytosis. Heating the sensitized serum at 56° C. for thirty minutes destroyed its ability to prevent phagocytosis. When serum from guinea pigs sensitized to egg albumin was used in the test in the presence of the specific antigen, phagocytic action was not inhibited. These observations demonstrate that a specific factor present in the serum of guinea pigs sensitized to certain species of bacteria is capable of inhibiting the phagocytic activity of normal guinea pig leukocytes in the presence of a filtrate of the specific organism. This phagocytosis inhibition test is similar to the leukocytolysis reaction and to studies of cell damage in tissue culture, but is simpler and can be performed more rapidly. B. S.

Influence of the Pituitary-Adrenal Axis on the Hemogram of Febrile White Rats. Hubler, W. L., Higgens, G. M., and Herrick, J. F.: Arch. Phys. Med. **33**: 391, 1952.

The effect of fever on the hematologic picture in white rats was studied. Hyperthermia induced a characteristic blood picture of eosinophilia, lymphopenia, and neutrophilia in normal white rats. In adrenalectomized animals, fever did not produce these changes. In hypophysectomized rats, the changes were the same as those observed in intact animals. These findings indicated that, in the intact animal, the altered blood picture associated with fever was due to adrenocortical stimulation.

Hyperthermia induced neutrophilia in adrenalectomized or hypophysectomized animals, but not in hypophysectomized-adrenalectomized animals. It was therefore postulated that either adrenocortical or pituitary hormone was responsible for the neutrophilia. The presence of adrenal medulla was found not to be necessary for the production of the usual hematopoietic response to fever in white rats. J. S.

Experimental Hypersensitivity. Relationship of Dosage to Serological and Pathological Responses Following Injection of Heterologous Protein. Moll, F. C., and Hawn, C. V.: Proc. Soc. Exper. Biol. & Med. **80**: 77, 1952.

Rabbits were injected intravenously with graded amounts of bovine serum gamma globulin. Complement and precipitin antibody titres were determined every two days until the animals were sacrificed on the fourteenth day. When the animals were sensitized with from 0.25 to 1.0 Gm. of gamma globulin per kilo of body weight there was a definite depression of complement titres between the eighth and tenth days. These animals invariably showed glomerular lesions attributable to hypersensitivity. When the amount of gamma globulin injected was less than 0.25 Gm. per kilo, the depression in complement was not regularly demonstrated and renal lesions were not found. Precipitin antibody was found in almost all injected animals, regardless of the amount of antigen which they received. Precipitins were usually demonstrable when complement was at its lowest level or immediately thereafter. There was no correlation between the level of circulating antibody and the incidence of renal lesions. The authors speculate that when the amount of antigen used is sufficiently large, the interaction of antigen and antibody is prolonged and severe enough to produce histological changes. In severe reactions, complement is utilized and depleted from the blood stream. The level of circulating antibody may be an index of excess antibody after circulating and tissue antigen have been neutralized and may bear no direct relation to the histological changes. B. S.

The Effect of ACTH and Cortisone on the Quantitative Precipitin Reaction. Malkiel, S., and Hargis, B. J.: J. Immunol. **69**: 217, 1952.

Rabbits were immunized by repeated intramuscular and intravenous injections of bovine serum albumin (BSA). Freund's adjuvant was given intramuscularly on the day of the first BSA injection as an additional antigenic stimulant. The test rabbits were given physiologically significant doses of either ACTH or cortisone prior to and during the course of immunization. Control animals received injections of the menstruum used in the preparation of the hormone suspensions. Antibody titres were measured by the quantitative precipitin method of Kabat and Mayer. Although the amount of specific antibody produced was rather low, there was a significant diminution in the amount of antibody produced by the hormone-treated group as compared with that produced by the control animals. The test rabbits were sacrificed and the adrenal glands and spleen were studied. Characteristic changes in the gross size and weights of these organs were observed showing that physiologically effective doses of the hormones had been administered. It was concluded that, when the quantitative precipitating technique was employed for measuring antibody content, it was possible to demonstrate that ACTH caused a marked diminution and cortisone an almost complete suppression of antibody titre. R. W.

Absence of Eosinopenic Response to ACTH Administration by the Aerosol Route in Normal Subjects. Gelfand, M. L., and Shearn, M. A.: Proc. Soc. Exper. Biol. & Med. **80**: 134, 1952.

Eosinophile counts were performed on 6 normal adult subjects before and four hours after the intramuscular injection of 25 mg. of ACTH. In each case, the decrease in circulating eosinophiles four hours after ACTH was 50 per cent or more. Several days later, 25 mg. of ACTH dissolved in distilled water or propylene glycol was administered by the aerosol route to each subject. Eosinophile counts were again done before and four hours after the administration of ACTH. Following the aerosol administration of ACTH, there was no significant drop in the number of circulating eosinophiles. These observations indicate that ACTH is not absorbed from the bronchopulmonary tree. B. S.

The Effect of Cortisone, Desoxycortisone, Adrenocorticotropic Hormone and Diphenhydramine Upon the Response of Albino Mice to General Anesthetics. Winter, C. A., and Flataker, L.: J. Pharmacol. & Exper. Therap. **105**: 358, 1952.

Cortisone and desoxycorticosterone acetate (D.C.A.) were administered subcutaneously once daily for three days to male mice. Eighteen hours after the last dose, ether anesthesia was given. In testing for the effect of ACTH on anesthesia, the drug was injected intraperitoneally immediately before anesthesia administration. Benadryl was given intraperitoneally thirty minutes before the anesthesia testing. The induction time for anesthesia in the animals treated with cortisone was elevated 25 per cent and the sleeping time was reduced 10 per cent. Desoxycorticosterone acetate did not affect induction time, but when both cortisone and D.C.A. were administered together, D.C.A. nullified the cortisone effect. Benadryl slightly prolonged induction time and slightly decreased sleeping time. Benadryl, however, did not "cancel out" the effect of cortisone, although it decreased the cortisone effect.

When the animals were anesthetized with intraperitoneal Evipal (a barbiturate), D.C.A. was without effect, cortisone or ACTH decreased the dura-

tion of anesthesia, and Benadryl potentiated the barbiturate. Cortisone, accordingly, is considered to be an analeptic drug, although it does not necessarily follow that the mechanism involved is the same as for caffeine and amphetamine. Since cortisone apparently did not antagonize Benadryl depression, whereas the usual analeptic drugs do, it is supposed that "the analeptic action of cortisone is of a different nature from that exhibited by these drugs." K.

Miscellaneous

Comparative Antigenic Potency of Killed Irradiated Tubercle Bacilli and Living BCG Vaccine. Birkhand, K., and Darricarrere, R.: Proc. Soc. Exper. Biol. & Med. **79**: 387, 1952.

Groups of normal, tuberculin-negative guinea pigs were immunized with batches of killed irradiated tuberculosis vaccine or living BCG vaccine. From one to three months after the last intraperitoneal inoculation, the animals were injected intramuscularly with a virulent strain of tubercle bacilli. The postimmunization mortality rate was greater in the irradiated-vaccine-treated group than in the BCG-vaccine group. Larger tuberculin reactions were obtained in the BCG vaccine group than in the irradiated vaccine group. Following the virulent challenge inoculation, a more retarded increment in tuberculin hypersensitiveness was noted in the animals immunized with BCG vaccine than in those immunized with irradiated vaccine. Furthermore, a much slower development of lymphonodular hypertrophy was noted in the vicinity of the virulent inoculation in the BCG-immunized animals. Death from generalized and advanced tuberculosis occurred in 44 per cent of control nonimmunized animals, in 15.9 per cent of BCG-immunized animals, and in 31.4 per cent of irradiated vaccine animals. Pathologic studies of the surviving animals in each group revealed a more severe form of tuberculous peritonitis in the irradiated vaccine group. In the group immunized with BCG, 56.8 per cent of the animals were completely protected against the spread of the challenge inoculation. In contrast to this, none of the irradiated vaccine-immunized animals were completely protected. It was thus concluded that BCG vaccine has superior antigenic potency and greater protective value than a vaccine consisting of tubercle bacilli killed by irradiation. B. S.

The Use of Adjuvants in Studies on Influenza Immunization. II. Increased Antibody Formation in Human Beings Inoculated With Influenza Virus Vaccine in a Water-in-Oil Emulsion. Salk, J. E., Bailey, M. L., and Laurent, A. M.: Am. J. Hyg. **55**: 439, 1952.

One hundred fifty-three young adults were injected intramuscularly with an emulsion containing several mixed strains of types A, A′, and B viruses, mineral oil, and Arlacel A emulsifier, or with the same virus mixture in salt solution. The incidence of local reactions in the group treated with emulsified vaccine was no greater than in the control group. An additional group of 173 medical students were also injected primarily for antibody response studies. Serologic studies demonstrated superior antibody formation in the emulsion-treated group after the second postinoculation week, reaching maximal levels by the sixth week. Antibody levels in those treated with adjuvant were persistently high at 6 months, with only a few individuals showing slight decline over the three-month levels. Although the Lee strain was the only type B virus in the mixture, the resultant antibody produced by the emulsion also reacted with the Warner strain of type B virus. Whereas saline mixtures of the viruses induced only poor antibody responses to the Cuppett strain and

strain 283 of A virus (not in the vaccine), and even to FM 1 antigen (present in the vaccine), those injected with the emulsified virus mixture produced good antibody response to all these strains. Thus there "appears to be a broadening effect as well as an elevating effect of the adjuvant upon antibody response not only to the viruses contained in the vaccine but to the strains that appear to be somewhat more distantly related as well." The implication of these findings on the antigenic formula for types A and B viruses is discussed. K.

Cough Medication and Antihistaminic Drugs. Boyd, E. M.: Canad. M. A. J. **67**: 289, 1952.

Large numbers of rabbits, albino rats, and guinea pigs were given 0.5 to 50 mg. doses per kilo of body weight of Chlortrimeton (chlorprophenpyridamine maleate) subcutaneously. The amount of secretion from the respiratory tract was measured for three hours prior to and for four hours following the antihistamine injection. The secretions from an untreated control series were similarly measured in order to evaluate the effects of the drug upon respiratory secretions. It was found that Chlortrimeton in the dosage used had no significant effect upon the amount of secretion obtained from any of the animals studied. Large amounts of Chlortrimeton given by mouth produced no effect different from that observed following parenteral administration. These results, plus previous experiences with diphenhydramine, have convinced the author that antihistamines per se are of no value in the routine treatment of cough. It was concluded that they should be used only when specifically indicated. R. W.

Immunization of Rabbits With Type II Pneumococcal Polysaccharide. Morgan, P., Watson, D. W., and Cromartie, W. J.: Proc. Soc. Exper. Biol. & Med. **80**: 512, 1952.

Rabbits were injected intravenously or intradermally with small amounts of pneumococcal type II polysaccharide. Serum was obtained from each rabbit prior to the immunization injection and on the seventh or eighth day after the last injection. Immunized and control animals were then challenged with an intradermal injection of a fresh culture of pneumococcus type III. All control animals developed fever and edematous lesions. The test animals failed to develop these signs and were considered immune. It was found that 0.2 ml. of pooled rabbit immune serum protected mice against at least 10,000 LD of pneumococcus type II, but failed to protect them against pneumococcus type I. Pooled normal rabbit serum taken before the onset of the immunization injections afforded no protection to mice against pneumococcus type II or type I. The immune serum failed to give a precipitin reaction with the type II pneumococcal polysaccharide and did not agglutinate a suspension of killed type II pneumococcus. The authors suggest that previous failure to immunize rabbits with type specific polysaccharides may be attributed to the use of excess polysaccharide resulting in "immunological paralysis." B. S.

Studies on Passive Immunity in Poliomyelitis. V. Lansing Antibody Levels in Humans After Gamma Globulin Administration. Wood, W., Clark, E. M., McKendry, J. B. M., and Rhodes, A. J.: Proc. Soc. Exper. Biol. & Med. **80**: 522, 1952.

Six children and four adults with no demonstrable Lansing antibody were used as subjects. They were injected intramuscularly with gamma globulin from pooled human plasma in doses varying from 0.1 to 0.4 ml. per pound of

body weight. Blood was taken at frequent intervals for six weeks and tested for Lansing antibody. Following this, the subjects were fed similar or larger amounts of gamma globulin and tests for antibody were again performed for six weeks. A small amount of neutralizing antibody was detected in the undiluted serum of subjects inoculated with gamma globulin by the intramuscular route. When the sera were diluted, no antibody could be detected. Neutralizing antibody was present for two weeks or longer. Antibody could not be detected following the oral administration of the gamma globulin. It is possible that the small amounts of antibody produced in these subjects might be sufficient to protect human beings against virus entry through the pharynx or gastrointestinal tract. B. S.

A Nontoxic Detergent for Aerosol Use in Dissolving Viscid Bronchopulmonary Secretions. Miller, J. B., and Boyer, E. H.: J. Pediat. **40**: 767, 1952.

The sputum-liquefying quality of the aerosol mist of Triton A-20, a new detergent, was noted as a coincidental effect in a group of adult patients being treated with various aerosols for pulmonary tuberculosis. Triton A-20 was then tried in various types of chronic pulmonary diseases characterized by highly viscid sputum and was found to be an effective and dependable method of liquefying thick viscid retained pulmonary secretions. In acute laryngotracheobronchitis in children, it was much more effective than steam.

Animal experiments indicated that the drug was entirely nontoxic even at high concentrations and after prolonged exposure. J. S.

Studies on the Circulating Eosinophiles in Normal and Toxemic Pregnant Women. Bernstine, J. B., and DeAndino, A. M.: Am. J. Obst. & Gynec. **63**: 181, 1952.

Eosinophile counts were done on 35 pregnant women of whom 26 were toxemic and 9 were normal. The counts were made at various intervals during pregnancy and after delivery.

No significant differences were found in the circulating eosinophiles of the peripheral blood of the normal and toxemic patients. J. S.